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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/621,448	07/21/2000	MICHAEL R. O'DONOHUE	1533.1010002/SRL/CMb	4431

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EXAMINER
STEADMAN, DAVID J

ART UNIT	PAPER NUMBER
1652	21

DATE MAILED: 05/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application No.	Applicant(s)	
	09/621,448	O'DONOHUE ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 February 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7,8,18,20 and 21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1* is/are allowed.

6)☒ Claim(s) *8,18,20 and 21* is/are rejected.

7)☒ Claim(s) *7* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

Application Status

[1] Claims 1, 7, 8, 18, 20, and 21 are pending in the application.

[2] Applicant's cancellation of claims 6 and 19 and amendment to claims 1, 7, 8, 18, 20, and 21 in Paper No. 20, filed 02/19/02, is acknowledged.

[3] Applicant's arguments filed in Paper No. 20 have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[4] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Claim Objections

[5] Claim 18 is objected to as the claim uses inconsistent terminology. Claim 1 recites "phosphoglucose isomerase" and claim 18 recites "6-phosphoglucose isomerase". While it is known in the art that the terms are synonymous and therefore, are not unclear as to their meaning, it is suggested that applicant maintains consistency in the identification of the recited enzyme by replacing "6-phosphoglucose isomerase" in claim 18 with "phosphoglucose isomerase".

[6] The objections to claims 7 and 20 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is maintained for the reasons of record and the reasons stated below. The objections were fully explained in a previous Office action (see items 3 and 4 of Paper No. 19). Applicant argues (beginning at page 6 of Paper No. 20) that claims 7 and 20 further limit independent claims 1 and 18, respectively, as claims 7 and 20 specify the type of disrupted *pgi* gene, limiting the disrupted *pgi* gene to a mutant *pgi* gene. Applicant's arguments are not found persuasive. A disrupted *pgi* gene is necessarily a mutant, i.e., not a wild-type, form of the gene. Disrupting a gene involves altering the gene in such a way that the gene is no longer a wild-type gene and must therefore be a mutant gene. As a disrupted *pgi* gene is necessarily a mutant *pgi* gene, claims 7

and 20 do not further limit claims 1 and 18, respectively, and applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim Rejections - 35 USC § 112, Second Paragraph

[7] The rejection of claims 8 and 21 under 35 U.S.C. 112, second paragraph, is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in a previous Office action (see item 5 part a of Paper No. 19). Applicant argues (page 7 of Paper No. 20) the claims have been amended to recite "suicide vector". Applicant's argument is not found persuasive. Claims 8 and 21 fail to recite "suicide vector" as asserted by applicant. It is noted that insertion of the term "suicide" prior to "vector" in part (a) of claims 8 and 21 would appear to overcome this rejection.

[8] Claim 20 recites the limitation "said disrupted *pgi* gene" and claim 21 recites the limitation "said altered *Corynebacterium glutamicum* cell having a disrupted *pgi* gene". There is insufficient antecedent basis for these limitations in the claims. It appears that applicant intends for the limitation of a *C. glutamicum* having a disrupted *pgi* gene in claim 18 based on dependent claims 20 and 21. However, because this limitation is not present in the amended claim, the examiner has interpreted claim 18 as it is written.

Claim Rejections - 35 USC § 112, First Paragraph

[9] Claim 18 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 18 is drawn to a method of producing L-lysine, L-threonine, or L-isoleucine by culturing a genus of altered *C. glutamicum* cells having a decreased amount of 6-phosphoglucose isomerase enzyme activity, wherein the enzyme activity is decreased by any method. The claim is rejected because the genus of altered *C. glutamicum* cells having a decreased amount of 6-phosphoglucose isomerase enzyme

activity has not been adequately described in the specification. The specification discloses only a single representative species of such altered *C. glutamicum* cells, i.e., a *C. glutamicum* cell having a decreased amount of 6-phosphoglucose isomerase enzyme activity due to disruption of the *pgi* gene by homologous recombination. The specification provides no other representative species of the claimed genus of altered *C. glutamicum* cells. One of skill in the art would understand that the species of altered *C. glutamicum* cells have substantial variation within the genus as the species of the genus encompass not only those *C. glutamicum* cells having a decreased amount of 6-phosphoglucose isomerase enzyme activity due to disruption of the *pgi* gene, but also those species of *C. glutamicum* cells having alterations within the amino acid sequence of phosphoglucose isomerase or the promoter/enhancer elements controlling expression of the *pgi* gene. The single disclosed species is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

[10] The scope of enablement rejection of claim 18 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing L-lysine, L-threonine, or L-isoleucine by culturing an altered *C. glutamicum* cell having a decreased amount of 6-phosphoglucose isomerase enzyme activity due to a disrupted *pgi* gene, does not reasonably provide enablement for a method of producing L-lysine, L-threonine, or L-isoleucine by culturing an altered *C. glutamicum* cell having a decreased amount of 6-phosphoglucose isomerase enzyme activity, wherein the enzyme activity is decreased by any method is maintained for the reasons of record and the reasons stated below.

Undue experimentation would be required for a skilled artisan to make and/or use the claimed invention. Factors to be considered in determining whether undue experimentation is required, are summarized in *In re* Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art,

(6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s). The Factors most relevant to the instant rejection are addressed below.

- The claims are overly broad in scope: As written, claim 18 is so broad as to encompass a method of producing L-lysine, L-threonine, or L-isoleucine by culturing an altered *C. glutamicum* cell having a decreased amount of 6-phosphoglucose isomerase enzyme activity, wherein the enzyme activity is decreased by *any* method. The scope of the claim is not commensurate with the enablement provided by the disclosure with regard to the scope of *C. glutamicum* cells having a decreased amount of 6-phosphoglucose isomerase enzyme activity broadly encompassed by the claims. In this case, the claim is limited to a method of producing L-lysine, L-threonine, or L-isoleucine by culturing an altered *C. glutamicum* cell having a decreased amount of 6-phosphoglucose isomerase enzyme activity due to a disrupted *pgi* gene.
- The lack of guidance and working examples: The specification provides guidance for decreasing phosphoglucose isomerase enzymatic activity only by disruption of the encoding *pgi* gene. The specification fails to identify other methods that may be used to reduce said enzymatic activity.
- The high degree of unpredictability of the art: The single working example for decreasing phosphoglucose isomerase enzymatic activity by disruption of the encoding *pgi* gene by homologous recombination fails to provide a skilled artisan with the knowledge and guidance necessary for predictably decreasing phosphoglucose isomerase enzymatic activity by any method – including mutating the amino acid sequence of phosphoglucose isomerase to generate a polypeptide with decreased enzymatic activity and mutating the promoter and/or enhancer elements that control *pgi* gene expression to reduce the level of expressed phosphoglucose isomerase. As neither the prior art nor the instant specification provides guidance regarding such mutations, a skilled artisan would recognize the high degree of unpredictability for decreasing phosphoglucose isomerase enzymatic activity by any method.
- The amount of experimentation: While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for any modification to a *C. glutamicum* cell that results in decreased phosphoglucose isomerase enzymatic activity as encompassed by the instant claim. Due to the broad

scope of the claim, the lack of guidance and working examples, and the high degree of unpredictability associated with decreasing phosphoglucose isomerase enzymatic activity by any method, undue experimentation would be required for a skilled artisan to make the claimed invention.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re* Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re* Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Conclusion

[11] Claims 1, 7, 8, 18, 20, and 21 are pending.

[12] Claims 8, 18, 20, and 21 are rejected.

[13] Claim 7 is objected.

[14] Claim 1 is in condition for allowance.

[15] Claims 7, 8, 18, 20, and 21 would be allowable if rewritten to overcome the objection(s) and rejection(s) under 35 U.S.C. 112, first and second paragraphs, set forth in this Office action.

Applicant's amendment to claim 18 necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The Examiner can normally be reached Monday-Thursday from 6:30 am to 5:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX number for this Group is (703) 308-4242. Any inquiry of a general nature or relating to

the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman, Ph.D.
Patent Examiner
Art Unit 1652

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP 1600